

WHAT IS CLAIMED IS:

1. An isolated molecule comprising an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen.
2. The isolated molecule of claim 1, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.
3. The isolated molecule of claim 1, further comprising an identifiable moiety being conjugated to said antibody.
4. The isolated molecule of claim 3, wherein said identifiable moiety is selected from the group consisting of a member of a binding pair and a label.
5. The isolated molecule of claim 3, wherein said member of said binding pair is an antigen.
6. The isolated molecule of claim 3, wherein said label is selected from the group consisting of a fluorescent protein and an enzyme.

7. The isolated molecule of claim 1, further comprising a therapeutic moiety being conjugated to said antibody.

8. The isolated molecule of claim 7, wherein said therapeutic moiety is selected from the group consisting of a cytotoxic moiety, a toxic moiety, a cytokine moiety and a bi-specific antibody moiety.

9. The isolated molecule of claim 1, wherein said HLA-restricted antigen is a tumor HLA-restricted antigen.

10. The isolated molecule of claim 1, wherein said HLA-restricted antigen is a viral HLA-restricted antigen.

11. The isolated molecule of claim 1, wherein said HLA-restricted antigen is an autoimmune HLA-restricted antigen.

12. A pharmaceutical composition comprising a therapeutically effective amount of a molecule which comprises an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen, said molecule further comprises a therapeutic moiety being conjugated to said antibody.

14. The pharmaceutical composition of claim 12, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

16. The pharmaceutical composition of claim 12, wherein said HLA-restricted antigen is a tumor HLA-restricted antigen.

17. The pharmaceutical composition of claim 12, wherein said HLA-restricted antigen is a viral HLA-restricted antigen.

18. The pharmaceutical composition of claim 12, wherein said HLA-restricted antigen is an autoimmune HLA-restricted antigen.

19. A diagnostic composition comprising a molecule which comprises an antibody specifically bindable with a binding affinity below 20 nanomolar to

a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen, said molecule further comprises an identifiable moiety being conjugated to said antibody.

20. The diagnostic composition of claim 19, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

21. The diagnostic composition of claim 19, wherein said identifiable moiety is selected from the group consisting of a member of a binding pair and a label.

22. The diagnostic composition of claim 19, wherein said member of said binding pair is an antigen.

23. The diagnostic composition of claim 19, wherein said label is selected from the group consisting of a fluorescent protein and an enzyme.

24. The diagnostic composition of claim 19, wherein said HLA-restricted antigen is a tumor HLA-restricted antigen.

25. The diagnostic composition of claim 19, wherein said HLA-restricted antigen is a viral HLA-restricted antigen.

26. The diagnostic composition of claim 19, wherein said HLA-restricted antigen is an autoimmune HLA-restricted antigen.

27. An isolated molecule comprising a first polynucleotide encoding an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen.

28. The isolated molecule of claim 27, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

29. The isolated molecule of claim 27, further comprising a second polynucleotide being linked to said first polynucleotide and encoding an identifiable moiety.

30. The isolated molecule of claim 29, wherein said identifiable moiety is selected from the group consisting of a member of a binding pair and a label.

31. The isolated molecule of claim 29, wherein said member of said binding pair is an antigen.

32. The isolated molecule of claim 29, wherein said label is selected from the group consisting of a fluorescent protein and an enzyme.

33. The isolated molecule of claim 27, further comprising a second polynucleotide being linked to said first polynucleotide and encoding a therapeutic moiety.

34. The isolated molecule of claim 33, wherein said therapeutic moiety is selected from the group consisting of a cytotoxic moiety, a toxic moiety, a cytokine moiety and a bi-specific antibody moiety.

35. The isolated molecule of claim 27, wherein said HLA-restricted antigen is a tumor HLA-restricted antigen.

36. The isolated molecule of claim 27, wherein said HLA-restricted antigen is a viral HLA-restricted antigen.

37. The isolated molecule of claim 27, wherein said HLA-restricted antigen is an autoimmune HLA-restricted antigen.

38. A method of producing an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen, the method comprising:

immunizing a genetically engineered non-human mammal having cells expressing said human major histocompatibility complex (MHC) class I with a soluble form of a MHC class I molecule being complexed with said HLA-restricted antigen;

isolating mRNA molecules from antibody producing cells of said non-human mammal;

producing a phage display library displaying protein molecules encoded by said mRNA molecules; and

isolating at least one phage from said phage display library, said at least one phage displaying said antibody specifically bindable with said affinity below 10 nanomolar to said human major histocompatibility complex (MHC) class I being complexed with said HLA-restricted antigen.

39. The method of claim 38, wherein said non-human mammal is devoid of self MHC class I molecules.

40. The method of claim 38, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

41. The method of claim 38, wherein said HLA-restricted antigen is a tumor HLA-restricted antigen.

42. The method of claim 38, wherein said HLA-restricted antigen is a viral HLA-restricted antigen.

43. The method of claim 38, wherein said HLA-restricted antigen is an autoimmune HLA-restricted antigen.

44. The method of claim 38, wherein said soluble form of a MHC class I molecule is a single chain MHC class I polypeptide including a functional human β -2 microglobulin amino acid sequence directly or indirectly covalently linked to a functional human MHC class I heavy chain amino acid sequence.

45. A method of treating a cancer, the method comprising administering to a subject in need thereof a therapeutically effective amount of a molecule which comprises an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a tumor HLA-restricted antigen characterizing said cancer, said molecule further comprises a therapeutic moiety being conjugated to said antibody, said MHC class I molecule being selected matching to the endogenous MHC class I of the subject.

46. The method of claim 45, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

47. The method of claim 45, wherein said therapeutic moiety is selected from the group consisting of a cytotoxic moiety, a toxic moiety, a cytokine moiety and a bi-specific antibody moiety.

48. A method of treating a viral infection, the method comprising administering to a subject in need thereof a therapeutically effective amount of a molecule which comprises an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a viral HLA-restricted antigen characterizing a virus causative of said viral infection, said molecule further

comprises a therapeutic moiety being conjugated to said antibody, said MHC class I molecule being selected matching to the endogenous MHC class I of the subject.

49. The method of claim 48, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

50. The method of claim 48, wherein said therapeutic moiety is selected from the group consisting of a cytotoxic moiety, a toxic moiety, a cytokine moiety and a bi-specific antibody moiety.

51. A method of treating an autoimmune disease, the method comprising administering to a subject in need thereof a therapeutically effective amount of a molecule which comprises an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with an autoimmune HLA-restricted antigen, said molecule further comprises a therapeutic moiety being conjugated to said antibody, said MHC class I molecule being selected matching to the endogenous MHC class I of the subject.

52. The method of claim 51, wherein said MHC class I molecule is selected from the group consisting of HLA-A2, HLA-A1, HLA-A3, HLA-A24, HLA-A28, HLA-A31, HLA-A33, HLA-A34, HLA-B7, HLA-B45 and HLA-Cw8.

53. The method of claim 51, wherein said therapeutic moiety is selected from the group consisting of a cytotoxic moiety, a toxic moiety, a cytokine moiety and a bi-specific antibody moiety.

54. A method of making an immunotoxin, the method comprising ligating a first polynucleotide encoding an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen in frame with a second polynucleotide encoding a toxin moiety, so as to obtain a ligated polynucleotide and expressing said ligated polynucleotide in an expression system so as to obtain said immunotoxin.

55. The method of claim 54, wherein said HLA-restricted antigen is selected from the group consisting of a tumor HLA-restricted antigen, a viral HLA-restricted antigen and an autoimmune HLA-restricted antigen.

56. A method of making an immunolabel, the method comprising ligating a first polynucleotide encoding an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility

complex (MHC) class I being complexed with a HLA-restricted antigen in frame with a second polynucleotide encoding an identifiable moiety, so as to obtain a ligated polynucleotide and expressing said ligated polynucleotide in an expression system so as to obtain said immunolabel.

57. The method of claim 56, wherein said HLA-restricted antigen is selected from the group consisting of a tumor HLA-restricted antigen, a viral HLA-restricted antigen and an autoimmune HLA-restricted antigen.

58. A method of making an immunolabel, the method comprising ligating a first polynucleotide encoding an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen in frame with a second polynucleotide encoding an identifiable moiety, so as to obtain a ligated polynucleotide and expressing said ligated polynucleotide in an expression system so as to obtain said immunolabel.

59. The method of claim 54, wherein said HLA-restricted antigen is selected from the group consisting of a tumor HLA-restricted antigen, a viral HLA-restricted antigen and an autoimmune HLA-restricted antigen.

10073301.021302

60. A method of detecting the presence and/or level of antigen presenting cells presenting a HLA-restricted antigen in a sample of cells, the method comprising:

interacting cells of said sample with an antibody specifically bindable with a binding affinity below 20 nanomolar to a human major histocompatibility complex (MHC) class I being complexed with a HLA-restricted antigen; and

monitoring said interaction, thereby detecting the presence and/or level of said antigen presenting cells presenting said HLA-restricted antigen.

61. The method of claim 60, wherein said HLA-restricted antigen is selected from the group consisting of a tumor HLA-restricted antigen, a viral HLA-restricted antigen and an autoimmune HLA-restricted antigen.

62. An isolated nucleic acid comprising a polynucleotide as set forth in SEQ ID NO:8.

63. An isolated protein comprising an amino acid sequence as set forth in SEQ ID NO:9.

64. An isolated nucleic acid comprising a polynucleotide encoding a polypeptide as set forth in SEQ ID NO:9.

40073301 011002